Consensus criteria for chronic rhinosinusitis disease control: an international Delphi Study*

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Abstract

Background: Chronic rhinosinusitis (CRS) disease control is a global metric of disease status for CRS. While there is broad acceptance that it is an important treatment goal, there has been inconsistency in the criteria used to define CRS control. The objective of this study was to identify and develop consensus around essential criteria for assessment of CRS disease control.

Methods: Modified Delphi methodology consisting of three rounds to review a list of 24 possible CRS control criteria developed by a 12-person steering committee. The core authorship of the multidisciplinary EPOS 2020 guidelines was invited to participate.

Results: Thirty-two individuals accepted the invitation to participate and there was no dropout of participants throughout the entire study (3 rounds). Consensus essential criteria for assessment of CRS control were: overall symptom severity, need for CRS-related systemic corticosteroids in the prior 6 months, severity of nasal obstruction, and patient-reported CRS control. Near-consensus items were: nasal endoscopy findings, severity of smell loss, overall quality of life, impairment of normal activities and severity of nasal discharge. Participants' comments provided insights into caveats of, and disagreements related to, near-consensus items.

Conclusions: Overall symptom severity, use of CRS-related systemic corticosteroids, severity of nasal obstruction, and patient-reported CRS control are widely agreed upon essential criteria for assessment of CRS disease control. Consideration of near-consensus items to assess CRS control should be implemented with their intrinsic caveats in mind. These identified consensus CRS control criteria, together with evidence-based support, will provide a foundation upon which CRS control criteria with widespread acceptance can be developed.

Key words: chronic rhinosinusitis; control, EPOS, consensus, Delphi, outcome measure

Introduction

Control of a disease implies that disease manifestations and how they impact the patient are at acceptable levels [1]. Because acceptability does not necessarily imply resolution, control is an important and commonly used metric of disease status and treatment response for incurable, chronic conditions [2]. For decades, the concept of disease control has been used in this manner for the assessment of asthma, with control being explicitly

recognized as the goal of asthma treatment [3-5]. Disease control is also used in the assessment of - and as a goal of treatment for - allergic rhinitis [6]. The concept of control has similarly been proposed as an important goal of treatment for chronic rhinosinusitis (CRS) [7].

The concept of control has been historically applied to CRS by clinicians, investigators and patients in a manner indicating the extent to which manifestations of CRS are within acceptable limits and with control serving as the goal of treatment [8,9]. The exact criteria by which CRS control is judged, in contrast, has been inconsistent. The first formally proposed criteria for assessment of CRS control was by the 2012 European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) [10]. These criteria, which have largely been preserved in EPOS 2020, captured multiple dimensions of CRS, including not only patients' symptom severities but also the need for systemic corticosteroids and antibiotics as well as the presence of diseased mucosa on nasal endoscopy [10,11]. Currently, at least fifteen different sets of criteria have been used to date in the scientific literature to assess CRS control [8]. The lack of consistency in the criteria for such an important outcome measure and global metric of CRS disease status represents a significant problem for the field, both from the perspectives of patient care and scientific investigation. Several factors may explain the lack of consistently used criteria for CRS control. One important factor is that no CRS control guideline has been developed with specific attention to broad consensus building around the individual criterion. Even the EPOS CRS control criteria were developed as expert opinion without a formal consensus determination. In this study, we therefore sought to determine and build formal consensus around the criteria that are deemed most essential for assessment of CRS control, engaging the authorship of the multidisciplinary EPOS guidelines as participants. We believe that the findings of this study, which identify criteria broadly agreed upon to be essential for the assessment of CRS control, together with evidence-based support, will provide a foundation upon which CRS control criteria with wide-spread acceptance can be developed.

Materials and methods

Study design

This study was designed with the primary objective of developing consensus around the criteria that are essential in determining CRS disease control using modified Delphi methodology. Because the first proposed criteria for the assessment of CRS disease control were in the EPOS guidelines, a multidisciplinary position paper on CRS, this study was designed to be implemented within the context of the EPOS authorship. A steering committee was organized consisting of the study organizers (ARS and CH), the EPOS 2020 steering committee, any EPOS authors involved in the development of the EPOS CRS control criteria, as well as one patient advocate from the EPOS 2020 authorship group - a total of 12 steering committee members. The steering committee developed a long list of statements, each summarizing a specific criterion for the assessment of CRS control. This long list was then presented to all participants as possible options for CRS control criteria. Participants, who were invited from the core EPOS 2020 authorship group, were then asked to participate in a modified Delphi process to develop consensus around criteria essential for the assessment of CRS control.

Modified Delphi process

The design of the modified Delphi process was established by the steering committee prior to study commencement to be consistent with fundamental elements of Delphi methodology (anonymity, iterative, controlled feedback) and methodology used in prior studies and consensus statements [12,13]. The modified Delphi process was implemented electronically in REDCap through the University of Cincinnati and was specifically designed to have three rounds. All core EPOS 2020 authors and steering committee were invited to participate. Although invitations were made as "an author of the 2020 EPOS guidelines to participate," quasi-anonymity was maintained by not sharing who ultimately participated or individual-level scores/data. In each round, participants were asked to rate their agreement with each statement from the long list identifying a specific CRS disease manifestation as essential to the assessment of CRS control on a 9-point Likert scale (agreement score): strongly disagree (1), disagree (3), neutral (5), agree (7), and strongly agree (9). To minimize the risk of presentation bias, statements were presented to participants in four different possible orders, each of which represented a random shuffling of the order in which statements were finalized by the steering committee.

In every round, a text box for each statement was provided in which comments could be made by the participant. Participants were instructed that these comment boxes reflected their opportunity to provide feedback, express their reasoning for their agreement scores and/or sway the opinion of their fellow participants. At the end of the first round, participants were also provided with a text box in which they could recommend additional CRS disease manifestations for inclusion in the subsequent Delphi rounds. Participants were given 3 weeks to complete each round.

At the end of each round, cumulative group-level results (agreement scores and comments) for each statement were compiled and sent to each participant; each participant was also provided with their own agreement scores for each statement so they could directly compare their ratings with group-level results. Participants were then asked to return any additional comments to the organizers. Participant comments were incorporated, where deemed appropriate, into the implementation of later rounds of the modified Delphi. There are many ways that con-

Table 1. Statements presented to participants for consensus in the assessment of CRS control.

Assessment of overall symptom severity attributed to CRS is essential for the routine assessment of CRS control.
Assessment of overall quality of life attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of nasal obstruction attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of nasal (anterior/post-nasal) discharge attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of smell loss attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of facial pain/pressure attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of ear discomfort (fullness/pressure/pain) attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of impaired sleep attributed to CRS is essential for the routine assessment of CRS control.
Assessment of severity of emotional/mood disturbance attributed to CRS is essential for the routine assessment of CRS control.
Assessment of use of short-course antibiotics (used for antibacterial properties) for CRS within the last 6 months is essential for the routine assessment of CRS control.
Assessment of use of long-term antibiotics (e.g. macrolides, used for anti-inflammatory properties) within the last 6 months for CRS is essential for the routine assessment of CRS control.
Assessment of use of systemic corticosteroids within the last 6 months for CRS is essential for the routine assessment of CRS control.
Assessment of use of steroid-eluting stents within the last 6 months for CRS is essential for the routine assessment of CRS control.
Assessment of use of biologics within the last 6 months for CRS is essential for the routine assessment of CRS control.
Assessment of prior endoscopic sinus surgery is essential for the routine assessment of CRS control.
Assessment of the extent of prior endoscopic sinus surgery is essential for the routine assessment of CRS control.
Assessment of nasal endoscopy findings (e.g. presence of edema, nasal polyps, or drainage) are essential for the routine assessment of CRS control.
Assessment of radiographic/imaging findings of the paranasal sinuses are essential for the routine assessment of CRS control.
Assessment of the degree to which CRS interferes with a patient's ability to perform normal activities (e.g. at work/school/home) is essential for the routine assessment of CRS control.
Assessment of occurrence of acute exacerbations of CRS within the last 6 months is essential for the routine assessment of CRS control.
Assessment of the severity of lower airway symptoms (e.g. hyperresponsiveness or asthma exacerbation) that is associated with their CRS is essential for the routine assessment of CRS control.
The patient's self-assessment of their own CRS control is essential for the routine assessment of CRS control.
Assessment of occurrence or future risk of CRS-related medication side effects is essential for the routine assessment of CRS control.
Assessment of occurrence of orbital or intracranial complications of CRS is essential for the routine assessment of CRS control.

sensus has been defined in Delphi methodology [13], from which our a priori definition of consensus for a statement after each round was developed as: a mean agreement score of ≥7 or ≤3, with less than 10% of participants as outliers (defined as having agreement score >2 Likert points away from the mean). When a statement reached consensus, it was no longer considered in subsequent rounds. "Near consensus" was defined as reaching the mean agreement score criterion for consensus but not the outlier criterion.

Assumptions, definitions, and instructions to participants

Prior to commencement of the study, the steering group agreed upon several assumptions and definitions that would establish the context of the modified Delphi process for all participants. CRS disease control was broadly defined as the extent to which CRS disease manifestations are within acceptable limits and achievement of CRS control was recognized as the goal of treatment. The steering group also developed additional specific instructions that were given to all participants prior to commencement of the modified Delphi, which are described in the "Delphi instructions for study participants" section of the Supplemental Materials.

Statistical analysis

All analyses were performed using the statistical software package R (www.r-project.org) [14]. Standard descriptive statistics (mean, standard deviation [SD], median and range) were calculated. Stability of participants' responses from one round to the next was calculated based on descriptive statistical analyses of changes in agreement scores for each item as well as a 2-way mixed effects intraclass correlation coefficient (ICC) [15]. Consistency of agreement scores from round to round was deemed to be moderate ($0.50 \leq ICC < 0.75$), good ($0.75 \leq ICC < 0.90$) or excellent ($0.90 \leq ICC$) [15].

Results

List development

A long list of possible CRS criteria was developed by the steering committee through a pre-planned process including meetings

Table 2. Agreement scores for items in Round 1 of Delphi.

Item*	Mean score	Median	Range	# of outliers (>2pts from mean)
1. Overall symptom severity**	8.4	9	3 – 9	1
2. Systemic corticosteroids**	8.3	9	5 – 9	2
3. Nasal obstruction**	8.1	9	3 – 9	3
4. Patient-reported control**	7.9	8	7 – 9	0
5. Nasal endoscopy findings***	7.8	9	3 – 9	4
6. Overall QOL***	7.8	9	3 – 9	6
7. Impairment of normal activities***	7.5	8	3 – 9	6
8. Smell loss***	7.4	8	3 – 9	7
9. Nasal discharge***	7.1	7	3 – 9	6
10. Sleep impairment***	7.1	7	4 – 9	9
11. Occurrence of AECRS	6.9	7	3 – 9	14
12. Facial pain/pressure	6.7	7	1 – 9	9
13. Severity of lower airway symptoms	6.7	7	3 – 9	13
14. Short course antibiotics	6.5	7	1 – 9	14
15. Use of biologics	6.5	7	1 – 9	18
16. Long-term antibiotics	6.1	7	1 – 9	8
17. Emotional/mood disturbance	6.1	6.5	1 – 9	12
18. Occurrence/future risk of med side effects	6.1	6.5	1 – 9	14
19. Prior ESS	5.8	5.5	1 – 9	18
20. Ear discomfort	5.5	5.5	1 – 9	13
21. Occurrence orbital/intracranial complications	5.5	6	1 – 9	23
22. Extent of prior ESS	5.3	5	1 – 9	18
23. Steroid-eluting stents	4.3	5	1 – 9	11
24. Radiographic/imaging findings	4.0	3	1 – 9	15

* Items sorted according to agreement score

** Reached full criteria for consensus

*** Reached mean score criteria for consensus

and discussion among the steering committee. The details of this process are described in the "Long list development" section of the Supplemental Materials. After completion of this process, a final list of 24 items was generated (Table 1).

Delphi results

Of the 41 individuals who were invited to participate, 32 agreed to participate in the first round. This consisted of 29 otolaryngologists, 2 patient advocates and 1 general practitioner. Invitations were sent for Round 1 in January 2023, for Round 2 in March 2023, and for Round 3 in May 2023.

The agreement scores for each statement after Round 1 of the modified Delphi are shown in Table 2 and Figure 1. The overall symptom severity score, the need for systemic corticosteroids for CRS in the prior 6 months, the severity of nasal obstruction and the patient's assessment of their own CRS control (patient-reported CRS control) all reached consensus as essential for the assessment of CRS control. The overall symptom severity score had the highest mean agreement score (mean: 8.4, median: 9) while patient-reported control was the only item reaching consensus with no outliers (Table 2).

After Round 1, CRS disease manifestations reaching near consensus as essential for the assessment of CRS control included nasal endoscopy findings, overall QOL, impairment of normal activities, smell loss, nasal discharge, and sleep impairment. Participants' comments from Round 1 related to these near consensus items are provided in Supplemental Table 1. No additional statements were added to the long list for subsequent rounds based on participants' feedback after round 1.

All 32 individuals who participated in the first round of the modified Delphi also participated in the second round. The agreement scores for each statement after Round 2 of the modified Delphi are shown in Table 3 and Figure 2. No statement reached consensus in Round 2 as essential for the assessment of CRS control. CRS disease manifestations reaching near consensus were smell loss, nasal endoscopy findings, overall QOL, impairment of normal activities, and nasal discharge. Participants' comments from Round 2 related to these near consensus items are provided in Supplemental Table 2. From Round 1 to Round 2, the mean change in agreement scores over all items was 1.4 points (SD: 1.6 points) in either direction, with a median change of 1 point. From Round 1 to Round 2, there was at least moderate consistency (ICC≥0.50) in how participants rated 14 out of the 20 statements (Table 4).

All 32 individuals who participated in the first and second rounds of the modified Delphi also participated in the third round, so there was no dropout in participation throughout the entire study. The agreement scores for each statement after Round 3 of the modified Delphi are shown in Table 5 and Figure 3. Similar to Round 2, no statement reached consensus in Round 3 as essential for the assessment of CRS control. CRS disease manifestations reaching near consensus in Round 3 were nasal endoscopy findings, smell loss, overall QOL, impairment of normal activities, and nasal discharge. Participants' comments from Round 3 related to these near-consensus items are provided in Supplemental Table 3. From Round 2 to Round 3, the mean change in agreement scores over all items was 1.1 points (SD: 1.4 points) in either direction, with a median change of 1 point. From Round 2 to Round 3, there was at least moderate consistency (ICC≥0.50) in how participants rated 16 out of the 20 statements (Table 6).

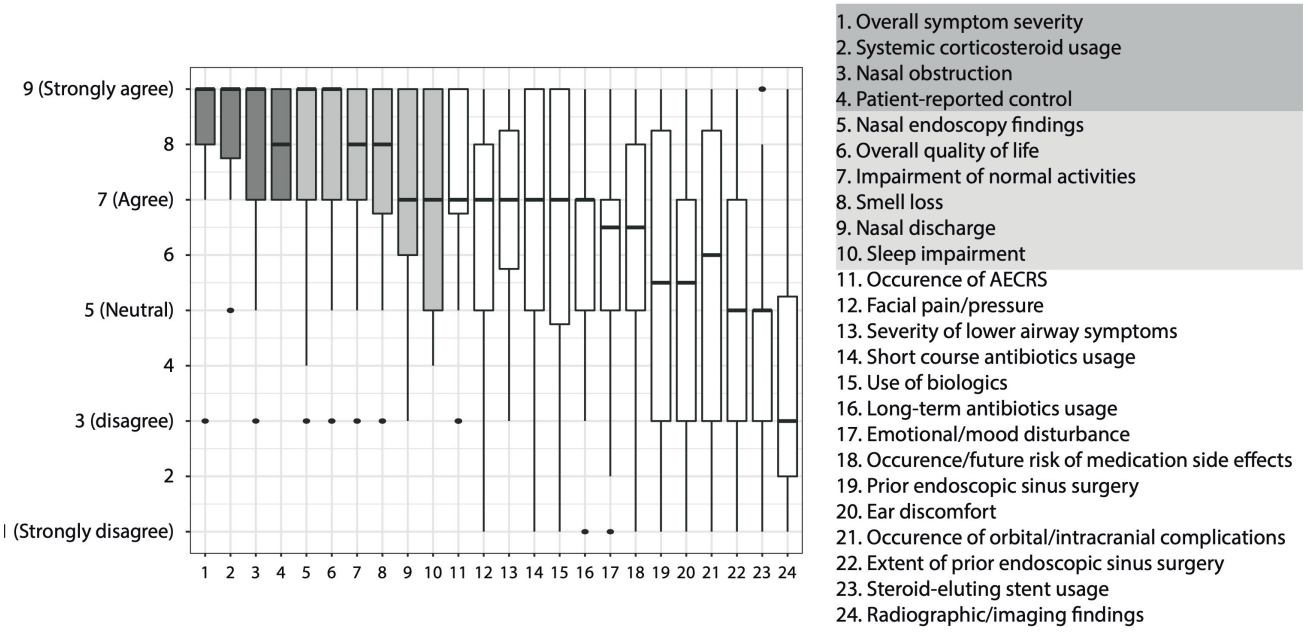

Figure 1. Box-and-whisker plots of agreement scores for each statement for the first round of the Delphi. Items reaching consensus are shaded/highlighted in dark grey. Items meeting mean score criteria—but not full criteria—for consensus are shaded/highlighted in light grey.

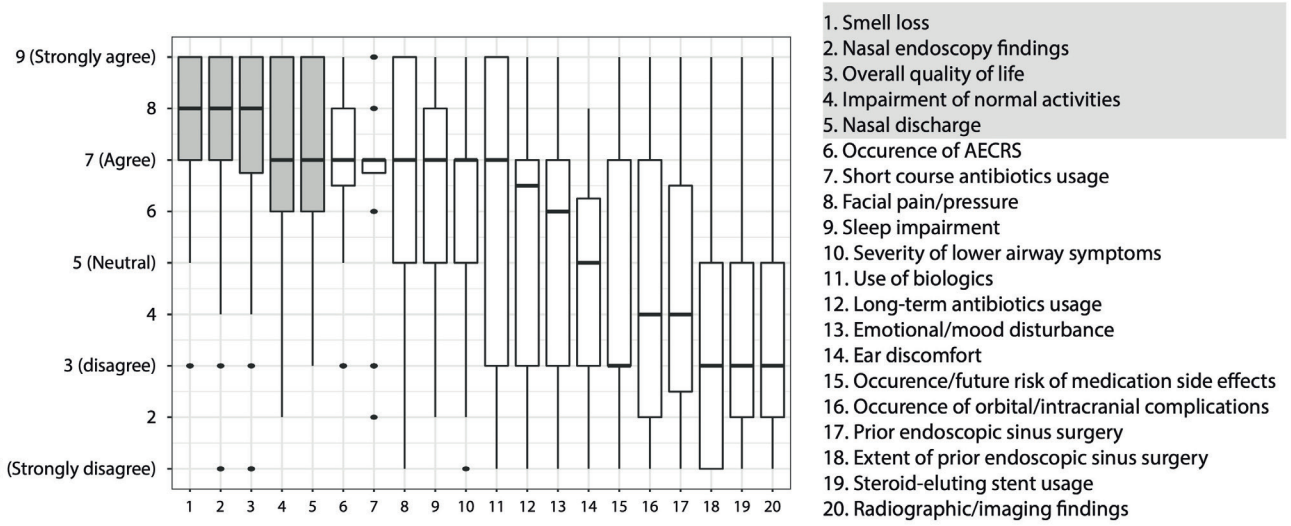

Figure 2. Box-and-whisker plots of agreement scores for each statement for the second round of the Delphi. Items meeting mean score criteria—but not full criteria—for consensus are shaded/highlighted in light grey.

Items reaching consensus and near consensus

Through three rounds of the modified Delphi, consensus was reached on the following items as being essential in the assessment of CRS control: overall symptom severity score, the need for systemic corticosteroids for CRS in the prior 6 months, the severity of nasal obstruction and patient-reported CRS control. Consensus on these items was reached during the first round, while items reaching near consensus—nasal endoscopy findings, smell loss, overall QOL, impairment of normal activities, and nasal discharge—were remarkably consistent across all three rounds (Table 7). Across the three rounds, participants' ratings demonstrated good or excellent consistency for nasal discharge (ICC=0.92) and nasal endoscopy (ICC=0.78), but moderate consistency for smell loss (ICC=0.52), overall QOL (ICC=0.72) and activity impairment (ICC=0.56). Participants' comments at each round (Supplemental Tables 1-3) offer insights into reasons why near consensus statements did not reach formal consensus.

Discussion

Inconsistency in the application of a concept or terminology

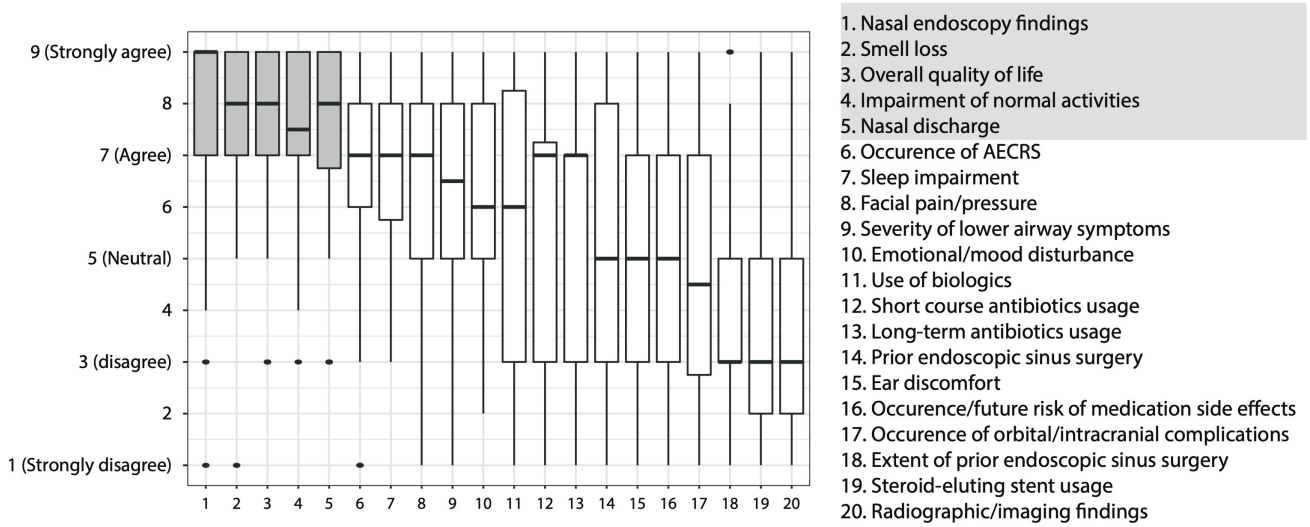

Figure 3. Box-and-whisker plots of agreement scores for each statement for the third round of the Delphi. Items meeting mean score criteria - but not full criteria - for consensus are shaded/highlighted in light grey.

Table 3. Agreement scores for items in Round 2 of Delphi.

Item*	Mean score	Median	Range	# of outliers (>2pts from mean)
1. Smell loss**	7.6	8	3 – 9	4
2. Nasal endoscopy findings**	7.2	8	1 – 9	6
3. Overall QOL**	7.1	8	1 – 9	6
4. Impairment of normal activities**	7.1	7	2 – 9	6
5. Nasal discharge**	7.0	7	3 – 9	7
6. Occurrence of AECRS	6.7	7	3 – 9	11
7. Short course antibiotics	6.4	7	2 – 9	9
8. Facial pain/pressure	6.4	7	1 – 9	14
9. Sleep impairment	6.2	7	2 – 9	14
10. Severity of lower airway symptoms	6.1	7	1 – 9	12
11. Use of biologics	6.0	7	1 – 9	18
12. Long-term antibiotics	5.7	6.5	1 – 9	16
13. Emotional/mood disturbance	5.5	6	1 – 9	15
14. Ear discomfort	4.7	5	1 – 8	12
15. Occurrence/future risk of med side effects	4.5	3	1 – 9	19
16. Occurrence orbital/intracranial complications	4.5	4	1 – 9	21
17. Prior ESS	4.4	4	1 – 9	17
18. Extent of prior ESS	3.8	3	1 – 9	16
19. Steroid-eluting stents	3.6	3	1 – 9	11
20. Radiographic/imaging findings	3.6	3	1 – 9	12

* Items sorted according to agreement score

** Reached mean score criteria for consensus

Table 4. Comparison of agreement scores between Round 1 and Round 2.

Item	Mean change* (SD)	Median change*	Range of change*	ICC**
1. Smell loss	1.1 (1.3)	1	0 – 6	0.60
2. Nasal endoscopy findings	1.1 (1.4)	1	0 – 7	0.68
3. Overall QOL	1.1 (1.4)	1	0 – 6	0.69
4. Impairment of normal activities	1.1 (1.3)	1	0 – 5	0.65
5. Nasal discharge	0.6 (0.9)	0	0 – 3	0.85
6. Occurrence of AECRS	1.5 (1.7)	1	0 – 6	0.35
7. Short course antibiotics	1.7 (1.5)	2	0 – 6	0.43
8. Facial pain/pressure	1.7 (1.3)	2	0 – 4	0.46
9. Sleep impairment	1.7 (1.9)	1	0 - 6	0.28
10. Severity of lower airway symptoms	1.0 (1.3)	1	0 – 5	0.74
11. Use of biologics	1.4 (1.7)	1	0 – 6	0.68
12. Long-term antibiotics	1.6 (1.8)	1	0 – 8	0.41
13. Emotional/mood disturbance	1.6 (1.6)	1	0 – 6	0.54
14. Ear discomfort	1.7 (1.6)	1	0 – 6	0.40
15. Occurrence/future risk of med side effects	1.8 (1.8)	1.5	0 – 6	0.67
16. Occurrence orbital/intracranial complications	1.5 (1.5)	1	0 – 6	0.79
17. Prior ESS	1.9 (2.1)	2	0 – 8	0.54
18. Extent of prior ESS	1.8 (1.9)	1.5	0 – 8	0.64
19. Steroid-eluting stents	1.4 (1.3)	1.5	0 – 5	0.65
20. Radiographic/imaging findings	1.5 (1.3)	2	0 – 4	0.64

*Absolute value of change, with a participant's change in score in either direction (increasing or decreasing) considered the same

**ICC = intraclass correlation coefficient, 2-way mixed effects model

Table 5. Agreement scores for items in Round 3 of Delphi.

Item*	Mean score	Median	Range	# of outliers (>2pts from mean)
1. Nasal endoscopy findings**	7.7	9	1 - 9	5
2. Smell loss**	7.6	8	1 - 9	4
3. Overall QOL**	7.4	8	3 – 9	5
4. Impairment of normal activities**	7.4	7.5	3 - 9	6
5. Nasal discharge**	7.2	8	3 - 9	6
6. Occurrence of AECRS	6.8	7	1 - 9	11
7. Sleep impairment	6.7	7	3 – 9	10
8. Facial pain/pressure	6.2	7	1 – 9	10
9. Severity of lower airway symptoms	6.1	6.5	1 – 9	13
10. Emotional/mood disturbance	6.0	6	2 – 9	15
11. Use of biologics	5.8	6	1 – 9	19
12. Short course antibiotics	5.8	7	1 - 9	17
13. Long-term antibiotics	5.7	7	1 – 9	32
14. Prior ESS	5.2	5	1 – 9	22
15. Ear discomfort	5.1	5	1 – 9	16
16. Occurrence/future risk of med side effects	5.0	5	1 – 9	19
17. Occurrence orbital/intracranial complications	4.6	4.5	1 – 9	18
18. Extent of prior ESS	4.1	3	1 – 9	32
19. Steroid-eluting stents	3.8	3	1 – 9	13
20. Radiographic/imaging findings	3.4	3	1 – 9	11

* Items sorted according to agreement score

** Reached mean score criteria for consensus

Table 6. Comparison of agreement scores between Round 2 and Round 3.

Item	Mean change* (SD)	Median change*	Range of change*	ICC**
1. Nasal endoscopy findings	0.5 (0.4)	0	0 – 7	0.82
2. Smell loss	1.2 (1.7)	1	0 – 8	0.36
3. Overall QOL	1.2 (1.2)	1	0 – 4	0.68
4. Impairment of normal activities	1.3 (1.6)	1	0 – 7	0.44
5. Nasal discharge	0.7 (0.9)	0	0 – 2	0.83
6. Occurrence of AECRS	1.5 (1.8)	1	0 – 6	0.37
7. Sleep impairment	1.4 (1.5)	1	0 – 5	0.49
8. Facial pain/pressure	1.1 (1.5)	0	0 – 6	0.63
9. Severity of lower airway symptoms	0.9 (1.3)	0.5	0 – 5	0.75
10. Emotional/mood disturbance	1.4 (1.3)	1	0 – 6	0.63
11. Use of biologics	1.0 (1.1)	1	0 – 4	0.84
12. Short course antibiotics	1.2 (1.8)	0	0 – 6	0.53
13. Long-term antibiotics	1.2 (1.5)	1	0 – 5	0.71
14. Prior ESS	1.6 (1.8)	1	0 – 7	0.63
15. Ear discomfort	1.3 (1.3)	1	0 – 4	0.64
16. Occurrence/future risk of med side effects	1.3 (1.6)	1	0 – 6	0.70
17. Occurrence orbital/intracranial complications	0.5 (0.7)	0	0 – 2	0.95
18. Extent of prior ESS	1.0 (1.1)	1	0 – 4	0.83
19. Steroid-eluting stents	1.1 (1.5)	0	0 – 5	0.63
20. Radiographic/imaging findings	0.9 (1.3)	0	0 – 4	0.74

* Absolute value of change, with a participant's change in score in either direction (increasing or decreasing) considered the same

**ICC = intraclass correlation coefficient, 2-way mixed effects model

in healthcare or science can slow and prevent its adoption by promoting confusion, misunderstanding and miscommunication among patients, healthcare providers and researchers. The inconsistent application of the disease control concept to CRS has suffered in this manner and the consequent underutilization of CRS disease control is especially problematic because it has been broadly identified as an important outcome measure [16]. It may be postulated that more common usage of this important global outcome measure could arise from development of criteria that are supported by both evidence and broad consensus for their essential place in the assessment of CRS control. While studies have been performed to identify the relative significance of individual CRS disease manifestations to CRS control, no study has yet sought to determine and develop formal consensus around the CRS disease manifestations that are deemed most essential by key stakeholders in the assessment of CRS control. In this study we used Delphi methodology to develop and identify formal consensus among the core authors of the multidisciplinary EPOS guidelines around the essential criteria of CRS control. We found that overall symptom severity, the use of systemic corticosteroids for CRS, severity of nasal obstruction, and patients' own assessments of their CRS control (patient-reported CRS control) achieved formal consensus as essential criteria in the assessment of CRS control. Although not reaching formal consensus, nasal endoscopy findings, overall QOL, activity impairment and the severities of smell loss and nasal discharge reached near-consensus as essential criteria for the assessment of CRS control.

Previous studies have suggested that a significant degree of consistency among key stakeholders - physicians and patients

Table 7. Top scoring statements reaching consensus or near-consensus.

Statements reaching full consensus criteria
Assessment of overall symptom severity attributed to CRS is essential for the routine assessment of CRS control.
Assessment of use of systemic corticosteroids within the last 6 months for CRS is essential for the routine assessment of CRS control.
Assessment of severity of nasal obstruction attributed to CRS is essential for the routine assessment of CRS control.
The patient's self-assessment of their own CRS control is essential for the routine assessment of CRS control.
Statements close to consensus (reaching mean agreement score criteria but not full criteria)
Assessment of nasal endoscopy findings (e.g. presence of edema, nasal polyps, or drainage) are essential for the routine assessment of CRS control.
Assessment of severity of smell loss attributed to CRS is essential for the routine assessment of CRS control.
Assessment of overall quality of life attributed to CRS is essential for the routine assessment of CRS control.
Assessment of the degree to which CRS interferes with a patient's ability to perform normal activities (e.g. at work/school/home) is essential for the routine assessment of CRS control.
Assessment of severity of nasal (anterior/post-nasal) discharge attributed to CRS is essential for the routine assessment of CRS control.

- may exist for what CRS control means and how it is assessed. For example, there is overlap in nasal symptom severity as one of the most important CRS control determinants for both physicians and patients [17,18]. Among patients, providers and researchers, there is consistency in considering the achievement of CRS control as the goal of treatment [8,9]. Among rhinologists of different backgrounds, there is remarkable consistency in how patients' CRS control is judged and consistency in the CRS disease manifestations that are most associated with their control assessments [19]. These results demonstrate that consistency in the concept of CRS control exists among key stakeholders and that the active pursuit of consensus CRS control criteria is achievable.

In this study, we identify several CRS disease manifestations that have consensus as essential criteria for the assessment of CRS control, and they include overall symptom severity, the severity of nasal obstruction, CRS-related systemic corticosteroid usage, and patient-reported CRS control. Consensus around these CRS control criteria is supported by prior studies establishing their importance as CRS outcome measures and targets of treatment. Symptom burden is the most significant CRS disease manifestation that affects patients, as well as how they perceive their CRS and their treatments [18,20]. To that end, overall symptom severity was developed to assess global CRS symptom burden [21], validated to be reflective of patients' perception of their CRS as mild, moderate and severe [22], and correlates with EPOS guideline-based classification of CRS control [23]. In fact, CRS symptom burden is tightly associated with how patients assess their own CRS control [24], with nasal symptoms—especially nasal obstruction— as the disease manifestation most dominantly associated with how patients assess their own CRS control [17,18,25]. Nasal obstruction severity in particular is a primary determinant of how physicians assess CRS disease control [17,19]. Our determination of consensus around the need for systemic corticosteroids as a CRS control criteria is also consistent with known practice patterns. CRS-related oral corticosteroid usage is associated with how physicians assess CRS control [17-19], and this practice is supported by evidence. CRS-related systemic corticosteroids usage has been shown to be an important outcome measure reflective of CRS disease burden [26,27] and a source of risk for morbidity from corticosteroid-associated adverse outcomes [28,29]. Patient-reported CRS control was the only item that reached consensus with no outliers, which is consistent with the importance placed on it in a recent study showing patient-reported CRS control to be the factor most associated with how rhinologists assess CRS control [19]. Patient-reported CRS control has been previously validated as an outcome measure reflective of CRS disease burden and QOL [30]. Because it directly reflects the patient's perspective of their disease, it has been proposed for inclusion in CRS control assessment as a means of better aligning patient perspectives with physician-derived guidelines [31].

We also identified several CRS disease manifestations that reached near consensus as essential criteria for CRS control. The significance of diseased mucosa on nasal endoscopy as a CRS control criterion - and by direct extension an independent target of treatment - has historically been a source of controversy. Previous studies have shown that nasal endoscopy findings have a weak - or no - correlation with patients' CRS symptom burden [32-36]. Studies have also shown that the nasal endoscopy criterion rarely changes the EPOS-based CRS control classification, while additionally serving as a primary source of discordance with how patients view their own CRS control [23,31]. In contrast to these perspectives, at least one study has shown that nasal endoscopy findings may have an especially important role in CRS control assessment when it is unclear whether symptoms are correctly being attributed to CRS by providing objective evidence of active disease [19]. This point was reflected in comments made by our study participants. Other comments echoed the theme that diseased mucosa on nasal endoscopy is a predictor of worsening of symptoms and disease

status in the future, although study participants who disagreed with this view commented on the lack of evidence to support the assertion. The diagnostic symptoms of smell loss and nasal discharge, both of which have been established to be important to CRS patients as targets of treatment [20], also did not reach full consensus as essential CRS control criteria. While the severity of nasal discharge has been shown to be a strong determinant of both patient-reported and rhinologist-assessed CRS control, the severity of smell loss has not [17,19,37]. Comments from participants pointed out that the smell loss may often be secondary and redundant to severe nasal obstruction and discharge, that smell loss may be most important for only the subset of patients with nasal polyps, or that permanent smell loss may occur in the setting of CRS without necessarily being an indicator of the active disease process. In contrast to the significance placed on nasal discharge severity in prior studies of CRS control [17,19,37], comments made against nasal discharge as an essential CRS control criterion indicated primary objections to the inclusion of post-nasal drainage. Although post-nasal drainage has been reported to be a very common symptom of CRS [38], participants' comments have argued for the non-specificity of post-nasal drainage, which may also be caused by other conditions. Activity impairment, which has been included in at least one CRS control assessment tool [17], also did not reach full consensus as essential. Its significance as a reflection of QOL was mentioned in comments both as evidence for its essentiality as well as its redundancy to other criteria (and hence its non-essentiality). Another point raised was that previously described associations of CRS-related productivity loss or activity impairment with emotional disturbance may indicate it is not necessarily a direct manifestation of CRS [39-41]. Interestingly, the need for short-term CRS-related antibiotics, and the severity of facial pain and sleep disturbance - all of which are included EPOS CRS control criteria - did not even reach near consensus. While CRS-related antibiotics have previously been considered an indirect measure of acute exacerbations of CRS [42], comments by Delphi participants indicated disagreement with its inclusion due to the lack of evidence to support short-term antibiotics as a treatment for CRS (43). Comments by Delphi participants also raised concerns about the non-specificity of facial pain and sleep disturbance, which while important to CRS could also be confounded by other comorbidities [44-46].

Our study has important implications for the future development of CRS control criteria and guidelines, the success of which will depend on broad acceptance of the contents. The results of our study now illustrate for the first time, consensus around essential criteria for the assessment of CRS control. Moreover, we also demonstrate quantitatively the degree of agreement around other possible CRS control criteria. In particular, for criteria reaching near-consensus, we have demonstrated not only the general state of opinions regarding their importance but also reasons for discrepancies in participants' opinions, all of which may provide opportunities for further study as well as provide avenues for reconciling disagreements about their inclusion in CRS control criteria.

This study should be interpreted within the constraints of its limitations. While the core EPOS authorship reflects a multidisciplinary group, the backgrounds of those who participated were heavily skewed towards otorhinolaryngology. Although the explicit views of CRS patients on CRS control have been studied qualitatively in the past [9], only two CRS patients participated in this Delphi study. Moreover, only one general practitioner participated while other stakeholders such as pulmonologists were not represented. Our study did not consider the means (e.g. scales) for measuring CRS control criteria. This was an intentional aspect of our study design to focus the consensus building around the criteria for CRS control. Our modified Delphi methodology also did not include any live or in-person discussions, which may have increased the chances that consensus would be reached for more statements. However, the intentional omission of live discussion in our design was to maintain anonymity and for the practical consideration of difficulty in assembling a quorum of participants. Finally, our modified Delphi was designed specifically to have 3 rounds rather than being open-ended, with study completion determined by strict stopping criteria defining stability in the lack of consensus for each item. While strict and formal stopping criteria may have more greatly ensured a true lack of consensus where consensus was not achieved, the performance of this study in an open-ended manner related to number of rounds may have led to dropout and ultimately the artificial achievement of consensus through attrition of participants.

Conclusion

Despite the many definitions by which CRS control has been assessed, there is remarkable consistency among key stakeholders in the individual criteria that are essential in the assessment of CRS control. Consensus CRS control criteria include overall symptom severity, the need for CRS-related systemic corticosteroids, nasal obstruction severity and patient-reported control. Near-consensus essential criteria - which have cogent arguments for and against - include nasal endoscopy findings, severity of smell loss, severity of nasal discharge, activity impairment and overall QOL. The identification of these consensus and near-consensus CRS control criteria will allow more focused investigation to support their incorporation into a broadly accepted definition for CRS control.

Authorship contribution

ARS and CH: concept of study, study design, steering group member, collection of data, analysis of results, write up of manuscript, critical review of all contents. WJF, VJL, PWH, RCK,

SR, STS, MBS, JM, PG, and TT: steering group member, study design, performance of the study, critical review of all results and manuscript. IA, WTAL, FMB, AC, NAC, JC, LDG, MD, RJH, LK, AK, BNL, CM, CMP, DR, RJS, BAS, TLS, PVT, and LZ: performance of the study, critical review of all results and manuscript.

Conflict of interest

The authors declare that they have no conflicts of interests regarding the publication of this paper.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Delphi instructions for study participants

1. The objective of this exercise is to identify CRS manifestations that are essential components of assessing CRS control. We define essential as an item of such importance to the concept of control that assessment of control would be meaningless without it.
2. All statements are intended for application to patients who already have a guideline-based established, known diagnosis of CRS.
3. Control is intended for application to all CRS patients (for example, this is not specific to any endotype or phenotype and it is intended for all CRS severities)
4. We assume that intranasal saline and topical corticosteroids are standard of care treatments so their use is not a reflection of control (or lack thereof).
5. CRS control assessment is intended to be a component of the typical/normal/routine assessment of CRS patients, cross-sectionally and longitudinally
6. We are not considering the scales (for example, VAS, Likert scale) used to measure components of control.
7. We are not considering what thresholds will apply to any items to be considered essential (for example, the number of surgeries or treatments, levels of severity of symptoms)
8. We are not restricting how many items can be considered essential at this stage and are considering each item independently.

Long list development

Prior to the first steering committee meeting, the organizers performed a literature search on the topic of disease control in asthma and CRS, with relevant articles downloaded and posted in a shared online folder available to all steering committee members to read and review. Steering committee members were also invited to add any other literature they felt was pertinent. Two steering committee meetings were planned for list development with the option for more meetings if needed, and an a priori quorum was defined as greater than 50% attendance. The first steering committee meeting was held in July 2022, which was attended by 9 out of the 13 steering committee members. During this meeting a list of possible statements regarding criteria for CRS control, around which consensus would be developed, was generated. After the meeting, this preliminary list was circulated electronically among all steering committee members. The organizers then revised the exact wordings of these statements with feedback received from all steering committee members. A second steering committee was held in October 2022, which was also attended by 9 out of the 13 steering committee members. At this meeting, a tentatively final list of statements each specifying a distinct CRS manifestation to be considered for assessment of CRS control was determined. After this meeting, the list of statements was again circulated to all steering committee members for feedback and input in relation to wording, from a which a final list was generated

Supplemental Table 1. Participant comments for "near-consensus" statements in Round 1 of the modified Delphi.

Nasal endoscopy findings
• "Accept nothing le.ss than perfect as 'optimal'"
• "So many factors to consider in relation to nasal endoscopy. First, I don't think that most of us target nasal endoscopy findings with our treatments in a manner that is independent of CRS symptoms. So if it is not an independent target of CRS treatment, what does treatment of nasal endoscopy findings achieve? Does it reduce any kind of tangible impairment or risk to the patient? I don't think there is any evidence to suggest that is case. On the other hand, I understand that nasal endoscopy findings may help convince health care providers that the other CRS manifestations (for example, symptoms) are truly due to CRS. But if we are starting our assessment of CRS control criteria from the place that we already are attributing these criteria/disease manifestations to CRS, then I think the nasal endoscopy could be unnecessary."
• "Endoscopy is the true measure of 'CRS' and maybe be normal in a symptomatic patient.....but maybe rhinitis or non-sinus origins"
• "Clinical practice is a balance between endoscopic control and patient perception of symptom control"
Overall QOL
• "Not global QOL"
• "Similar to OSS, I think overall QOL is too narrow of a global measure (although better than OSS) compared to patient's assessment of their own CRS control "
• "Choice of HRQoL tool important"
Impairment of normal activities
• "The association between mood/emotional disturbance and CRS impact on productivity and activity makes me question whether this is an *essential* component of control rather than a reflection of the impact of a disease modifier."
• "This might be redundant depending on how 'an overall assessment of QoL' is interpreted
• "Really too detailed"
Smell loss
• "Depends strongly of how much the patient cares/bothers about this symptom. Wide range of complaints"
• "I don't think individual symptoms are needed if overall symptom control is rated by the patient. But without an overall measure then individual symptoms become more important"
• "This is tough for me. It is an important symptom of CRS but this symptom seems to be redundant to nasal obstruction and drainage, and it seems to be occur as an end-stage symptom of CRS. Also, how do we judge this in the setting where patients have permanent OD (e.g., complication of prior ESS or some other cause)?"
• "Other causes of non-CRS olfactory dysfunctional are common."
Nasal discharge
• "I don't think individual symptoms are needed if overall symptom control is rated by the patient. But without an overall measure then individual symptoms become more important"
• "Post nasal drip does not have a predictive value"
Sleep impairment
• "Only if the sleep impairment is clearly related to the CRS. Before rating this point to be essential I would go for a sleep exam and rule out apnea"
• "Poor sleep quality has been shown to be the symptom most greatly associated with decreased QOL and improvement in sleep quality also the symptom most greatly associated with improvement in QOL. However, this symptom can obviously be confounded by other conditions. If this symptom can be assessed as being attributed to CRS, then I think it's important to assess due to the QOL impact."
• "This might be redundant depending on how 'an overall assessment of QoL' is interpreted

Supplemental Table 2. Participant comments for "near-consensus" statements in Round 2 of the modified Delphi.

Smell loss
• "Still believe this to be an important issue" • "Smell loss is a symptom of advanced CRS, which reflects a small portion of the general CRS population, and by the time that patients have this symptom, they have other more common symptoms (like nasal obstruction and nasal drainage) quite severely so the severity of smell loss becomes redundant. To me, as a less common symptom of CRS, this is adequately captured in the overall symptom severity criterion that we have. Also, what do you do for patients who have impaired sense of smell due to COVID or for iatrogenic reasons? Do you classify them as being one step closer to uncontrolled CRS? I think allowing patients to lump this into overall symptom severity (when attribute it to a modifiable symptom of their CRS--and patients are definitely savvy enough to know when this is the case) also makes more sense to me for this reason." • "Loss of smell can be only an important part of the disease" • "One of the two most important outcomes according to patients" • "Diagnostic Sx and a must - so many view this as a control Sx"
Nasal endoscopy findings
• "The criteria for disease control typically fall into one of two categories: impairment and risk. For anyone who believes that nasal endoscopy findings are an essential criterion for judging CRS control, where is the evidence? How does the presence of nasal endoscopy findings impair the patient or impart risk? How does choosing to treat nasal endoscopy findings *help the patient*? I reflexively want to include this as a CRS control criterion but I struggle to find real evidence/justification besides just saying that it feels right." • "This is particularly important. All roads to a successful follow the same pathway of reduction of T1/T2 inflammation and restoration of epithelial function. Restoration of epithelial function and barrier integrity thus appears crucial for improvement. Thus assessment of epithelia status as a proxy for epithelial function is essential. Conversely to pulmonology, we can assess this directly and should strongly consider including it. We need to adapt recommendations form other disciplines to our own needs and diseases, not try and make our disease fit an assessment scheme designed for another disease, such as asthma." • "Important to balance against patient perception" • "I know studies suggest otherwise. But for me, deciding on the control of disease without having used an endoscope is counter-intuitive" • "Endoscopic findings do not necessarily show a parallelism with symptoms, but they allow to assess the current status and be helpful to predict what is going to happen. e.g. one sees a type I polyposis after 6 months, and then a type II after another 6 months. Patient still has good nasal breathing, but we can already foresee the need of further / additional treatment" • "Surely naso-endoscopy would only be carried out if there was an indication? what relevance would such an intervention have if the patient were controlled?" • "If the patient feels great but the sinuses look bad, the disease is uncontrolled and symptoms usually follow shortly" • "Endoscopic findings of inflammation in the absence of complaints indicates a strong risk of progression" • "I think this is the best physical diagnosis tool that will help with assessment of control"
Overall QOL
• "There may be other reasons for decreased QOL." • "QOL is already covered by the criteria we are selecting. Overall QOL is redundant so I am disagreeing that it is a *critical* criterion that we should add to what we've already agreed upon. Also, looking forward to the future, how do we assess this distinct from other criteria like overall symptom severity?" • "Captures general severity of symptoms caused by CRS not captured otherwise." • "Disease-specific QoL is very important in my view; a more general (i.e. overall) QoL is less important for me." • "I think this is going to be captured by patient rating of control"
Impairment of normal activities
• "Sort of fits into the overall QOL appreciation. Also, most NP patients are surprisingly happy and not that depressed or anxious over their condition. Only element I double down on is sleep." • "Captured in QOL" • "I'm conflicted by inferences with ability to perform normal activities. I've seen too many studies that tie this to emotional disturbance (e.g. comorbid mood disorders) or comorbid migraine in the setting of CRS that I just don't fall on the side of activity impairment being a reflection of the CRS (I think it is more a reflection of other CRS disease modifiers)" • "Absence from work / school etc. will mainly depend on overall symptom score and may reflect the status of the CRS. However, should we consider that this is already 'reflected' in the overall symptom status, then we could join both questions (OSS including absenteeism)" • "Any work absence due to any disease process is a measure of both severity and control."
Nasal discharge
• "We know from multiple studies of patients' perspectives of CRS control that nasal drainage is a very important symptom criteria for patients judge their own control. Whether you disagree with the exact wording (e.g. include PND), the point I'd make is that nasal drainage/discharge is **important to patients**. And in my book, that makes it an important target for treatment (i.e., criteria for CRS control) for all CRS patients." • "I do not believe that nasal discharge (particularly posterior) is essential. How about rating this depending on color of mucous? yellowish-greenish is not the same then translucent. Also, sticky (glue-like) mucous may indicate loss of control of the disease." • "The combination of anterior and posterior makes this questions impossible to answer for me. Most patients after ESS have PND, something I always warn them for before surgery. Some patients experience PND as cumbersome and would therefore never achieve control if (physiological) PND is taken into account. For anterior discharge and especially thick discharge I think the severity can be important" • "One of the important symptoms of CRS" • "Not for the post-nasal discharge because its too non-specific and subjective" • "Post-nasal drip is a symptom with poor specificity" • "Diagnostic symptom of CRS"

Supplemental Table 3. Participant comments for "near-consensus" statements in Round 3 of the modified Delphi.

Nasal endoscopy findings
• "Only if clinically indicated by a deterioration" • "If the patient does not have symptoms but the mucosa is very inflamed I consider that uncontrolled and the symptoms will follow shortly. On the other hand perfectly normal endoscopy and a lot of symptoms also is an indication to carefully check what is wrong" • "Endoscopy is a direct measure of epithelial and mucosal status. In GI, the definition of control includes healing of mucosal lesions. This appears relevant to our disease model. Endoscopy is NOT considered in asthma - Endoscopy is actually not feasible in a symptomatic asthma patient. This partially explains why measures of disease activity in asthma are all indirect: FeNO, Eos, periostin. We should be prudent before letting asthma define our space, which is finally quite different despite the similarities." • "Any control assessment that didn't include endoscopy assessment would not be accepted by our peers and the profession"
Smell loss
• "This is of great importance to the patient" • "Some patients can have out of control CRS but still remain normosmic and I would consider those poorly controlled. In contrast, others feel great except for impaired olfaction and normal endoscopy and I would consider those controlled." • "I accept that it can be caused by other things but that also applies to nasal blockage, nasal discharge and facial pain/pressure and it is a verified cardinal symptom. Of course could be argued to be covered in overall symptom score in which case all individual symptoms should be dropped" • "I think this is end-type driven – i.e., more important in Type 2 / NP - harder to give a score for CRS in general" • "Some patients have long standing loss of sense of smell and do not recover." • "Diagnostic symptom - must be 'strongly agree'"
Overall QOL
• "I still think this is an important criterion of control but agree that it is indirectly covered by 'patient reported CRS control' Again with the retrospectoscope, I would have voted to include an initial question on a disease-specific measure such SNOT 22" • "Total quality of life is one step removed from CRS that impacts daily activities - the sensitivity to detect change will be less"
Impairment of normal activities
• "I still think this is an important criterion of control but agree that it is indirectly covered by 'patient reported CRS control'"
Nasal discharge
• "Diagnostic symptom - must be 'strongly agree'"